

70, L60 → V) (SEQ ID NO: 25), QNLLSNAVLPQFP (Ty 56-70, P64 → V) (SEQ ID NO: 28),  
~~QNLLSNAPQGPQFP (Ty 56-70, L65 → Q) (SEQ ID NO: 29), DYSQEQDSDPDSEQD (Ty~~  
~~448-462, Y451 → Q) (SEQ ID NO: 34), DYSYQQDSDPDSEQD (Ty 448-462, L452 → Q) (SEQ~~  
~~ID NO: 35), DYSYFQDSDPDSEQD (Ty 448-462, L452 → F) (SEQ ID NO: 36)].~~

### REMARKS

Applicants respectfully request entry of the instant amendment. The amended claims do not introduce new subject matter, nor do the amendments raise new issues of patentability. Entry of this amendment is respectfully requested. It is believed that entry of the amendment places the application into condition for allowance. If the Examiner decides to maintain the rejection of this application, entry of the amendment will reduce the number of issues remaining for appeal.

Claims 64-92 are currently pending in the instant application.

Claims 68, 71, 76, 79, 82, 85, 88 and 91-92 have been rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to convey to one skilled in the art that the inventor had possession of the claimed invention. In particular, the Examiner asserts that certain named amino acids at positions 4 and 6 of the formulas  $X_1LLSNX_2PLG$  and  $X_1LQDSX_2PDS$ , recited in claim 68, are not described in the instant specification. Applicants respectfully disagree with this rejection.

As an initial matter claim 92 is erroneously included in this rejection, because claim 92 ultimately depends from claim 64 and not claim 68. Claim 64 does not recite the formulas at issue in the Examiner's rejection. Thus, applicants assume this claim was inadvertently included in this rejection. Reconsideration and withdrawal of this rejection of claim 92 is respectfully requested.

Regarding claims 68, 71, 76, 79, 82, 85, 88 and 91, the Examiner asserts that position 4 as serine or aspartic acid and X<sub>2</sub> as methionine, leucine, threonine, isoleucine, serine and valine are not supported by the instant specification. Applicants respectfully disagree.

As to the assertion that position 4 as a serine or aspartic acid is not described in the specification, applicants respectfully direct the Examiner's attention to the two main peptides described throughout the specification as Ty 56-70 and Ty 448-462 and shown in Figure 7. The upper panel of Figure 7 shows the sequence of Ty 56-70. Based upon this figure and its description on page 6, lines 25-29, it is clear that the sequences recited in claim 68 begin with the P1 position which is shown as the boxed "I". As one counts to the fourth position after P1, a "S" (for serine) is shown. One skilled in the art can readily recognize that serine is a preferred amino acid at this position, based upon the assays carried out in Example II and shown in Figure 6 (see top line of data, showing immunogenicity measured as GM-CSF in pg/ml/24h.). If the Examiner now focuses attention on the lower panel of Figure 7, this panel shows the sequence of Ty 448-462. Based upon this figure and its description on page 6, lines 25-29, it is clear that the sequences recited in claim 68 begin with the P1 position which is shown as the boxed "Y". As one counts to the fourth position after P1, a "D" (for aspartic acid) is shown. One skilled in the art can readily recognize that aspartic acid is a preferred amino acid at this position, based upon the assays carried out in Example II and shown in Figure 9 (see top line of data, showing immunogenicity measured as GM-CSF in pg/ml/24h.). Thus, serine and aspartic acid at position 4 of the claimed sequences are fully supported by the specification and one skilled in the art would recognize these amino acids as highly preferred at the fourth position after P1.

As relates to the Examiner's position that X<sub>2</sub> as serine and threonine are not described in the specification because these amino acids are not "hydrophobic", applicants

respectfully direct the Examiner's attention to page 13, lines 26-29 of the specification. Here, X<sub>3</sub>, which is the sixth position of the claimed sequence (now claimed as X<sub>2</sub>), is described as:

any hydrophobic amino acid or hydroxyl amino acids.  
Examples of amino acids that may be used include, but are not limited to, leucine, isoleucine, methionine, valine, serine or threonine. (emphasis added).

Thus, X<sub>2</sub> as serine or threonine is described in the specification, so that one skilled in the art would readily recognize that these amino acids are within the scope of the invention as originally filed.

For these reasons, applicants respectfully request reconsideration and withdrawal of this §112, first paragraph rejection.

Claims 64-92 have been rejected under 35 U.S.C. §112, first paragraph, for the reasons set forth in paragraph 6 of the January 25, 1999 Official Action. In that Official Action, the rejection is described as being based on the Office Action dated April 29, 1998. In the April 1998 Office Action, the Examiner rejected claims 3-30, 56, 61 (all now cancelled) and claim 64 (pending, now amended) on the basis that single amino acid substitutions affect the biological activity of the peptide, according to several prior art references. Therefore, the Examiner has taken the position that:

Since:

- 1) the quantity of experimentation necessary of the claimed invention requires screening a multitude of peptides
- 2) the art teaches of the unpredictability of single amino acid substitutions have on a protein (i.e. Salgaller et al., Burgess et al., and Lazar et al);
- 3) peptides fail to bind or bind poorly despite the presence of an optimal motif (see Englehard);
- 4) peptide positions including P2, P3, P5-P7 and P9 of nonamer peptide are important for stable binding (see Parker et al)

a skilled artisan would be forced into undue experimentation to practice the claimed invention.

Applicants respectfully disagree with this rejection.

Applicants' response will address the claims in two separate groups. First, claims 64-67, 69-70, 72-75, 77-78, 80-81, 83-84, 86-87, 89-90 and 92 will be addressed. These claims are directed to specific enumerated and exemplified peptides and their use. As to these claims, no experimentation, let alone an undue amount, is necessary to carry out the invention with these peptides. There is no need to "screen a multitude of peptides". There is no need to consider the "unpredictability of single amino acid substitutions" or that "peptides fail to bind or bind poorly despite the presence of an optimal motif". The enumerated peptides of these claims are specifically exemplified in the specification (See Example II and Figures 6-12) and are shown to have appropriate immunogenic properties. There is no need to consider which amino acids should be used for P2 P3, P5-P7 and P9 of the peptide. In these claims, the peptides are shown in the specification and data is provided demonstrating immunogenic activity. The Examiner is respectfully directed to focus on Figures 6-12 which present data showing immunogenicity for the claimed peptides. Thus, applicants assert that these claims are enabled and that *no experimentation* is necessary to determine the peptides of the claims or to use the peptides as claimed. Reconsideration and withdrawal of this rejection of claims 64-67, 69-70, 72-75, 77-78, 80-81, 83-84, 86-87, 89-90 and 92 is respectfully requested.

As the above §112, first paragraph rejection relates to claims 68, 71, 76, 79, 82, 85, 88 and 91, applicants assert that no undue amount of experimentation is necessary to practice the invention as claimed. These claims relate to peptides having the formulas  $X_1LLSNX_2PLG$  and  $X_1LQDSX_2PDS$ , wherein  $X_1$  is methionine, leucine, isoleucine, tyrosine, valine, tryptophan

and phenylalanine; and X<sub>2</sub> is methionine, leucine, threonine, isoleucine, serine and valine. The specification provides specific teaching that the two variable amino acid positions can be any of the enumerated amino acids (page 13, lines 17-19 and lines 28-29). Examples of such variations at these positions are shown in Figure 6 for X<sub>1</sub>LLSNX<sub>2</sub>PLG, (i.e. the third and fourth lines show X<sub>1</sub> as a phenylalanine (“F”) and valine (“V”) respectively and on the twelfth line X<sub>2</sub> is shown as a valine (“V”)) and in Figure 9 for X<sub>1</sub>LQDSX<sub>2</sub>PDS, (i.e. the third line shows X<sub>1</sub> as a phenylalanine (“F”)). These representative examples led the inventors to conclude that the other named amino acids may be substituted at these positions without the loss of immunogenic activity. The Examiner appears to take the position that because some researchers have concluded certain amino acid substitutions affect immunogenicity, no amino acid substitution can be predicted. Applicants have not randomly selected amino acids for the first and fourth positions but rather have selected only those amino acids that exhibit structural, chemical or functional similarities to those experimentally identified as having the desired immunogenic properties. The limited number of amino acid substitutions claimed enable the skilled artisan to carry out the invention as it is claimed, without the need for undue experimentation. Thus, applicants assert that these claims meet the requirement of 35 U.S.C. §112, first paragraph. Reconsideration and withdrawal of this §112 rejection of claims 68, 71, 76, 79, 82, 85, 88 and 91 is respectfully requested.

Claims 69-79 have been rejected under 35 U.S.C. §112, second paragraph as lacking antecedent basis for the recitation of “the immunogenic peptide”. Applicants have amended the claims to address the Examiner’s concerns. Reconsideration and withdrawal of this §112 rejection is respectfully requested.

The instant claims are believed in condition for allowance, and early and favorable action by the Examiner is earnestly solicited. If the Examiner believes that issues may be resolved by a telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 415-8564.

**AUTHORIZATION**


No additional fee is believed to be necessary.

The Commissioner is hereby authorized to charge any additional fees which may be required for this amendment, or credit any overpayment to Deposit Account No. 13-4500, Order No. 2026-4205.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 2026-4205. A DUPLICATE OF THIS SHEET IS ATTACHED.

Respectfully submitted,

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By   
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Dated: November 15, 1999

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